

Amendments to the Specification:

At the end of the application, please replace the current Sequence Listing with the attached Sequence Listing.

Please add the following Heading after the paragraph ending on page 1, line 3:

BACKGROUND

Please add the following Heading after the paragraph ending on page 2, line 12:

SUMMARY

Please add the following headings and new paragraphs after the paragraph ending on page 3, line 27:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 represents a coding DNA sequence and corresponding polypeptide sequence according to the invention.

Figure 2A represents amino acids 545-684 (SEQ ID NO:1) of the gp160 envelope protein of HIV. The sequence is taken from a consensus sequence of 32 strains in the Swissprot database and is identical with the sequence of isolate ENV_HV1BR (Swiss-Prot P03377).

Figure 2B represents peptide sequences (SEQ ID NOs:3-6, their numbering corresponding to Figure 2A) of regions where structural analogies or homologies with IL-2 are present.

Figure 2C represents a linker oligopeptide (SEQ ID NO:2) convenient for linking the N- and C- terminal peptides of gp41 after removal of amino acids 604-615 or 598-622 of the gp160 envelope protein of HIV of Figure 2A.

Figure 2D represents oligopeptide sequences (SEQ ID NOs:15 and 16, their numbering corresponding to Figure 2A) that may be advantageously replaced by a linker in accordance with the invention.

Figure 3 represents amino represents amino acids 539-675 (SEQ ID NO:14) and the corresponding nucleotide sequence (SEQ ID NO:13) of the gp160 envelope protein of HIV. The sequence is taken from the reference strain HxB2 gp41, where amino acids 598 and 604 have been replaced with serine.

Figures 4A and 4B represent sequences (SEQ ID NOs:17 and 18) of two representative polypeptides according to the invention.

Figures 5A and 5B represent sequences (SEQ ID NOs:19 and 20) of two representative polypeptides according to the invention.

Figure 6 represents a polypeptide sequence (SEQ ID NO:21) illustrating the invention, with N-terminal truncation, and comprising the linker sequence of Figure 2C (SEQ ID NO:2).

Figure 7 represents the primer sequences used in the amplification of the gp41 N-helix and the introduction of the linker (SEQ ID NOs:9 and 10) and for the amplification of the C-helix (SEQ ID NOs:11 and 12).

Figure 8 is a chromatographic elution profile of the polypeptide of the invention on a Superdex 200 HR liquid chromatography column.

DETAILED DESCRIPTION OF EMBODIMENTS

Please replace the paragraph beginning on page 4, line 6, with the following rewritten paragraph:

Within another embodiment of the invention, the deleted oligopeptide is located in the region from ~~525 to 549~~ 593 to 617, in particular in the region from ~~530 to 542~~ 599 to 610, according to the numbering of SEQ ID NO 14 (Fig. 3).

Please replace the paragraph beginning on page 4, line 31, with the following rewritten paragraph:

The peptide sequence ~~of region 545-684 (SEQ ID NO 1)~~ (SEQ ID NO:1), reproduced ~~in the appended~~ in Figure ~~2A~~ 2A, is a gp41 consensus sequence of 32 HIV-1 strains in the Swiss Protein Database. This sequence is identical with the sequence of isolate ENV_HV1BR (Swiss-Prot P03377). ~~(32 HIV-1 strain SWISS-PROT).~~

Please replace the paragraph beginning on page 5, line 1, with the following rewritten paragraph:

The peptide sequence 540-675 (SEQ ID NO:14), ~~represented on~~ in Figure 3, ~~SEQ ID NO 14~~, is derived from ~~sequence of the gp41 of the HxB2 strain of HIV-1 virus (SWISS~~ PROT CODE: ENV_HV_1 B isolate ENV_HV1LW, Swiss-Prot Q70626), ~~wherein~~ where the cysteine amino acid residues ~~cysteine~~ in positions ~~530~~ 598 and ~~536~~ 604 have been replaced by the serine amino acid residues ~~serine~~. Immunodominant region refers to a peptide sequence ~~which~~ that induces, in a great majority of cases (for example in at least 7 cases out of 10 approximately), a humoral and/or cellular response of the immune system directed against ~~said the~~ the region after immunization with a protein containing ~~said the~~ the sequence or with a peptide essentially consisting of ~~said the~~ the sequence.

Please replace the paragraph beginning on page 6, line 24, with the following rewritten paragraph:

Wildtype oligopeptides that may be advantageously replaced by a linker in accordance with the present invention are represented by SEQ ID NO 15 and SEQ ID NO 16 (Figure 2D), ~~and are corresponding. These correspond respectively to sequences between positions 603 and to amino acids to 604 to 615, and between positions 558 and 598 to 622 of SEQ ID NO 1, and oligopeptides sequences between position 530 to 542 to amino acids 599 to 610 and between position 525 to 149 593 to 617 of SEQ ID NO 14.~~

Please replace the paragraph beginning on page 7, line 4, with the following rewritten paragraph:

In the appended Figure 2B, the peptide sequences of four regions of this region of gp41 555-557 (SEQ ID NO 3), 572-601 (SEQ ID NO 4), 590-620 (SEQ ID NO 5) and 628-663 (SEQ ID NO 6), are represented in which structural analogies and/or cross reactions were noted with IL-2. These regions are homologously found in the SEQ ID NO 14, ~~and are respectively corresponding~~ correspond to the peptide sequences found in positions ~~482-504, 499-529, 517-547, 555-590 550-572, 567-597, 585-615, and 623-658.~~

Please replace the paragraph beginning on page 8, line 1, with the following rewritten paragraph:

A modified polypeptide according to the instant invention is in particularly represented by the sequence SEQ ID NO 8 of Figure 1. This modified polypeptide has been derived from SEQ ID NO 14, wherein the oligopeptide sequence ~~between from~~ positions ~~531 to 542 599-610~~ has been replaced with a linker corresponding to SEQ ID NO 2 (Figure 2C), and the oligopeptide sequence ~~between from~~ positions ~~597 to 607 665-675~~ has been replaced

by a His-Tag. In these sequences, an additional mutation has been carried-out in position ~~528~~ 596 (numbering according to SEQ ID NO 14), wherein a ~~tryptophan~~ tryptophan residue has been replaced by an aspartate amino acid residue.

Please replace the paragraph beginning on page 11, line 21, with the following rewritten paragraph:

These oligonucleotide primers were designed to respectively introduce the sites for restriction enzymes NdeI and BamHI (twice underlined into the oligonucleotides primers sequences above). The sequences homologous to the gp41 gene ~~into~~ in both ~~oligonucleotides~~ oligonucleotide primers are written in ~~italie~~ italics. The oligonucleotide primer gp41-BamIL was also designed to introduce (1) the oligopeptide linker SGGRGGS (SEQ ID NO 2) to replace the deleted portion of the loop (corresponding to the once and twice underlined sequences) and (2) a mutation ~~to introduce in the~~ at position ~~528~~ 596 (protein numbering SEQ ID NO 14) ~~wherein~~ where a tryptophan has been replaced by an aspartate amino acid (bold triplet).